Title
Brief Report: Cystatin C-Based Estimation of Glomerular Filtration Rate and Association With Atherosclerosis Imaging Markers in People Living With HIV.

Journal
Journal of acquired immune deficiency syndromes (1999), 85(4)

ISSN
1525-4135

Authors
McClean, Mitchell
Buzkova, Petra
Budoff, Matthew
et al.

Publication Date
2020-12-01

DOI
10.1097/qai.0000000000002467

Published in final edited form as:

J Acquir Immune Defic Syndr. 2020 December 01; 85(4): 466–469. doi:10.1097/QAI.0000000000002467.

Cystatin C based estimation of glomerular filtration rate and association with atherosclerosis imaging markers in people living with HIV

Mitchell MCCLEAN[a], **Petra BUZKOVA**[b], **Matthew BUDOFF**[c], **Michelle ESTRELLA**[d], **Matthew FREIBERG**[e], **Howard N. HODIS**[f], **Frank PALELLA**[g], **Cecilia SHIKUMA**[h], **Wendy S. POST**[i], **Samir GUPTA**[a]

[a]Indiana University School of Medicine Indianapolis, Indianapolis, IN

[b]University of Washington, Seattle, WA

[c]Los Angeles Biomedical Research Institute at Harbor-UCLA, Torrance, CA

[d]University of California, San Francisco, CA and San Francisco VA Health Care System, San Francisco, CA

[e]Vanderbilt University School of Medicine, Tennessee Valley Veterans Affairs Medical Center Geriatric Research Education and Clinical Centers (GRECC), Nashville, TN

[f]Keck School of Medicine University of Southern California, Los Angeles, CA

[g]Northwestern University Feinberg School of Medicine, Chicago, IL

[h]John A. Burns School of Medicine, University of Hawai'i at Mãnoa, Honolulu, HI

[i]Johns Hopkins University School of Medicine, Baltimore, MD

Abstract

INTRODUCTION: Reduced estimated glomerular filtration rate (eGFR) is associated with increased risk of cardiovascular disease among people living with HIV (PLWH). It is unclear whether eGFR equations incorporating Cystatin C (CysC) measurements are more predictive of preclinical CVD than those using only creatinine (Cr).

OBJECTIVES: The study aimed to determine which of the three Chronic Kidney Disease Epidemiology (CKD-EPI) eGFR equations is most associated with carotid intima media thickness (CIMT) and coronary artery calcium (CAC) score.

METHODS: This cross-sectional analysis of pooled data from three large cohorts compared the associations between the three CKD-EPI eGFR equations (Cr, CysC, and Cr-CysC) with CIMT and CAC score using multivariable regression analysis. eGFR and CIMT were analyzed as

Correspondence: Dr. Mitchell McClean, Indiana University School of Medicine, Department of Medicine, Division of Infectious Diseases, Emerson Hall, 545 Barnhill Drive, suite 421 Indianapolis, IN 46202 USA phone: 317-274-8115, fax: 317-274-1587 mmcclean@iu.edu.

Conflicts of Interest: No conflicts of interest reported for all authors

Note: This work was presented in part at the 25th Conferences on Retroviruses and Opportunistic Infections (Boston, MA; 2018)

continuous variables. CAC scores were analyzed as a binary variable (detectable calcification versus nondetectable) and as a log10 Agatston score in those with detectable CAC.

RESULTS: 1487 participants were included, and of these 910 (562 HIV+, 348 HIV−) had CIMT measurements and 366 (296 HIV+, 70 HIV−) had CAC measurements available. In HIV− participants, GFR estimated by any CKD-EPI equation did not significantly correlate with CIMT or CAC scores. When PLWH were analyzed separately including HIV-specific factors, only GFR estimated using Cr-Cys C correlated with CIMT [β= −0.90, 95% CI (−1.67,−0.13) μm; p=0.023]. Similarly, eGFR correlated with Agatston scores only when using cystatin C-based eGFR [β= −8.63, 95% CI (−16.49,−0.77) HU; p=0.034]. Associations between other eGFR formulas and CAC did not reach statistical significance.

CONCLUSION: In PLWH, preclinical atherosclerosis may be more closely correlated with eGFR using formulae that incorporate CysC measurements than Cr alone.

Keywords

HIV-1; Cystatin C; Carotid Intima Media Thickness; Coronary Artery Calcium; Cardiovascular disease; Glomerular Filtration Rate

Introduction

Reduced estimated glomerular filtration rate (eGFR) is associated with an increased risk of cardiovascular disease (CVD) in both the general population[1, 2] and people living with HIV (PLWH)[3-5]. GFR estimating equations incorporating serum cystatin C, compared to those using solely serum creatinine, are more predictive of cardiovascular events and overall mortality in the general population[6] and of overall mortality in PLWH[4, 7-10]. We sought to determine whether cystatin C-based or creatinine-based estimates of GFR were more strongly associated with two measures of subclinical cardiovascular disease, which are predictors of cardiovascular events, namely carotid intima media thickness (CIMT) and coronary artery calcium (CAC)[11-17]

Methods

We conducted a cross sectional analysis of data pooled from three large observational cohorts of PLWH and HIV− uninfected (HIV−) controls [Veterans Aging Cohort Study (VACS), Multicenter AIDS Cohort Study (MACS), and Hawaii Aging with HIV-1 Cohort (HA)]. We used multivariable regression analysis to evaluate correlations between GFR with both CIMT (ultrasound measured at the right distal common carotid artery) and CAC scores measured by CT scanning. We performed these analyses using each of three CKD-EPI eGFR equations [creatinine (Cr), cystatin C (CysC), and both creatinine and cystatin C (Cr-CysC)][18, 19]. Serum CysC was quantified centrally using N Latex Cystatin C kit per manufacturer instructions (Seimens, Eschborn, Germany). Our models included the entire pooled cohort and included an interaction term between HIV serostatus and eGFR. Covariates in all models included demographic factors (age, sex, race/ethnicity) and CVD and kidney disease risk factors (systolic and diastolic blood pressure, history of diabetes, total cholesterol, LDL-C, HDL-C, triglycerides, smoking status, body mass index, hepatitis

C serostatus). We also constructed models in PLWH alone and included HIV-specific factors (CD4+ T cell count, HIV-1 RNA level, and history of antiretroviral medication use). CIMT, CAC, and CysC were centrally measured as previously described[20-22]; serum Cr was measured locally. eGFR and CIMT were analyzed as continuous variables. CAC scores were analyzed as a continuous variable using $\log_{10}$Agatston score in persons with detectable CAC. Statistical significance was defined as $P<0.05$.

Results

We included 1487 participants (945 HIV+, 542 HIV−). Of these 910 (562 HIV+, 348 HIV−) and 366 (296 HIV+, 70 HIV−) had CIMT and CAC measurements available, respectively (Supplementary Table 1). Among persons with CIMT measurements, 96.3% were male, 22.5% were Black, 11.9% Hispanic, 57.9% White, and 7.7% Asian. There were 4.3-5.4% with eGFR <60 mL/min/1.73m^2 and 25.1-52.3% had eGFR <90 mL/min/1.73m^2, depending on the eGFR formula used. Mean (SD) CIMT was 0.79 (0.15) mm (Supplementary Table 1).

Among persons with CAC measurements, 94% were male, 47% were Black, 9.6% were Hispanic, 31.5% were White, and 11.8% were Asian. There were 4.8-5.9% with eGFR <60 mL/min/1.73m^2 and 27-52.8% had eGFR <90 mL/min/1.73m^2, depending on the eGFR formula used. Of the 366 with CAC measurements, 176 (48.1%) had detectable CAC, with a mean (SD) $\log_{10}$Agatston score of 1.87 (0.79) (Supplementary table 1).

In the overall cohort including both PLWH and HIV− participants, neither creatinine nor cystatin C-based eGFR were associated with greater CIMT (Table 1). Of note, there was an interaction between HIV status and Cr based eGFR's relationship with CIMT (β (95% CI) = −1.32 (−2.49,−0.15), P=0.027). When PLWH were analyzed separately including HIV-specific factors, eGFR using Cr-Cys C model correlated with greater CIMT. In PLWH, each 10 mL/min/1.73m^2 lower in eGFR by Cr-CysC was associated with a 9.0 μm (95% CI, −1.67,−0.13 μm; P=0.023) greater CIMT. Associations with other eGFR formulas did not reach statistical significance.

Similarly, neither creatinine nor cystatin C based estimates of GFR were associated with greater Agatston scores in the cohort regardless of HIV serostatus (Table 2). However, when PLWH were analyzed separately including HIV-specific factors, eGFR correlated with higher Agatston scores only when using cystatin C-based eGFR. Each 10 mL/min/1.73m^2 decrease in CysC-eGFR was associated with a 0.086 higher $\log_{10}$Agatston score (95% CI .077,0.165; P=0.034). Associations between other eGFR formulas and CAC did not reach statistical significance. None of the GFR estimates were associated with CAC when analyzed as a binary variable (detectable vs non-detectable calcification), regardless of HIV serostatus.

Discussions

In this large and diverse cohort, estimates of GFR that incorporated CysC were more significantly correlated with CIMT measurements and Agatston scores in PLWH than GFR estimates without CysC. In PLWH, eGFR was inversely correlated to CIMT using Cr-CysC, but not with Cr or CysC; eGFR was inversely correlated with CAC Agatston scores using

CysC but not with Cr or Cr-CysC. This suggests that GFR estimating formulae incorporating cystatin C may be more useful to identify PLWH with subclinical CVD who are in greater need of aggressive CVD risk reduction. These results are consistent with several studies suggesting that cystatin C-based eGFR is more predictive of both CVD and mortality than Cr in PLWH[4, 8, 9, 23]. One study reported that CysC eGFR had the strongest association with cardiovascular events of the three CKD-EPI equations among PLWH[8]. To date, there has not been a study demonstrated that CysC-based eGFR in PLWH is more closely associated with greater CAC or CIMT than Cr-based eGFR. A recent study using CT angiography found a correlation between Cr-based eGFR and calcified coronary plaque and Agatston score in PLWH, but not in HIV− controls[5]. In our analysis, creatinine based eGFR did not correlate with higher Agatston scores, but cystatin C based eGFR did. This may be explained in part by different methodology of Agatson score measurement or differences in study population (their cohort was modestly younger and included more women).

Of note, our analysis did not consistently reveal a link between HIV infection itself and greater CIMT or CAC. Similarly, a recent large study suggests that HIV's association with CIMT may be age dependent, with middle-aged patients showing little association between HIV and CIMT[24]. Other studies have examined CIMT's association with HIV and some reported higher CIMT values among PLWH, while others found such an association only in certain subgroups of PLWH [15, 25, 26]. The addition of kidney function estimates in our models may also have minimized the relationship between HIV seropositivity and these imaging markers. Strengths of our study include having large samples of both PLWH and HIV− participants, use of standardized centrally-measured plasma cystatin C, CIMT, and CAC scores, and adjustment for other factors known to contribute to development of both renal and cardiovascular disease. However, our study is limited by having a predominantly male population with few having an eGFR <60 mL/min/1.73m^2. We did not have data on antiretroviral, blood pressure, and lipid-lowering medications, which may have confounding effects on kidney function. Finally, we could not assess causality in this cross-sectional analysis.

In conclusion, investigators studying the interplay between CVD and renal disease in PLWH should consider utilizing eGFR formulae that incorporate CysC since these may correlate more significantly with atherosclerosis in PLWH.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

This work was supported in part by the HIV-CVD Collaborative Data Coordinating Center, funded by the NIH/NHLBI R01HL095126. The MACS CVD2 study is funded by the National Heart, Lung and Blood Institute (NHLBI), R01 HL095129 (Post), with additional support from UL1 TR 001079 from the National Center for Advancing Translational Sciences (NCATS), a component of the National Institutes of Health (NIH) and NIH Roadmap for Medical Research. Data in this manuscript were collected by the Multicenter AIDS Cohort Study (MACS) with centers (Principal Investigators) at Johns Hopkins University Bloomberg School of Public Health (Joseph Margolick), U01-AI35042; Northwestern University (Steven Wolinsky), U01-AI35039; University of California, Los Angeles (Roger Detels), U01-AI35040; University of Pittsburgh (Charles Rinaldo), U01-AI35041;

the Center for Analysis and Management of MACS, Johns Hopkins University Bloomberg School of Public Health (Lisa Jacobson), UM1-AI35043. The MACS is funded primarily by the National Institute of Allergy and Infectious Diseases (NIAID), with additional co-funding from the National Cancer Institute (NCI). Targeted supplemental funding for specific projects was also provided by the National Heart, Lung, and Blood Institute (NHLBI), and the National Institute on Deafness and Communication Disorders (NIDCD). MACS data collection is also sup- ported by UL1 TR 001079 (JHU CTSA) and UL1-TR000124 (Harbor-UCLA CTSA). Website: http://www.statepi.jhsph.edu/macs/macs.html. The contents of this publication are solely the responsibility of the authors and do not represent the official views of the National Institutes of Health (NIH).

References

1. Budoff MJ, Rader DJ, Reilly MP, Mohler ER 3rd, Lash J, Yang W, et al. Relationship of estimated GFR and coronary artery calcification in the CRIC (Chronic Renal Insufficiency Cohort) Study. American journal of kidney diseases : the official journal of the National Kidney Foundation 2011; 58(4):519–526. [PubMed: 21783289]
2. Matsushita K, van der Velde M, Astor BC, Woodward M, Levey AS, de Jong PE, et al. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. Lancet 2010; 375(9731):2073–2081. [PubMed: 20483451]
3. Choi AI, Li Y, Deeks SG, Grunfeld C, Volberding PA, Shlipak MG. Association between kidney function and albuminuria with cardiovascular events in HIV-infected persons. Circulation 2010; 121(5):651–658. [PubMed: 20100969]
4. Choi A, Scherzer R, Bacchetti P, Tien PC, Saag MS, Gibert CL, et al. Cystatin C, albuminuria, and 5-year all-cause mortality in HIV-infected persons. American journal of kidney diseases : the official journal of the National Kidney Foundation 2010; 56(5):872–882. [PubMed: 20709438]
5. Cheru LT, Fitch KV, Saylor CF, Lu M, Hoffmann U, Lo J, et al. Mild renal impairment is associated with calcified plaque parameters assessed by computed tomography angiography in people living with HIV. AIDS 2019; 33(2):219–227. [PubMed: 30325774]
6. Shlipak MG, Matsushita K, Arnlov J, Inker LA, Katz R, Polkinghorne KR, et al. Cystatin C versus creatinine in determining risk based on kidney function. The New England journal of medicine 2013; 369(10):932–943. [PubMed: 24004120]
7. Yanagisawa N, Sasaki S, Suganuma A, Imamura A, Ajisawa A, Ando M. Comparison of cystatin C and creatinine to determine the incidence of composite adverse outcomes in HIV-infected individuals. Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy 2015; 21(2):84–89. [PubMed: 25456895]
8. Lucas GM, Cozzi-Lepri A, Wyatt CM, Post FA, Bormann AM, Crum-Cianflone NF, et al. Glomerular filtration rate estimated using creatinine, cystatin C or both markers and the risk of clinical events in HIV-infected individuals. HIV medicine 2014; 15(2):116–123. [PubMed: 24024499]
9. Driver TH, Scherzer R, Peralta CA, Tien PC, Estrella MM, Parikh CR, et al. Comparisons of creatinine and cystatin C for detection of kidney disease and prediction of all-cause mortality in HIV-infected women. AIDS 2013; 27(14):2291–2299. [PubMed: 23669156]
10. Roy SK, Estrella MM, Darilay AT, Budoff MJ, Jacobson LP, Witt MD, et al. Glomerular filtration rate and proteinuria associations with coronary artery calcium among HIV-infected and HIV-uninfected men in the Multicenter AIDS Cohort Study. Coron Artery Dis 2017; 28(1):17–22. [PubMed: 27611875]
11. Papita A, Albu A, Fodor D, Itu C, Carstina D. Arterial stiffness and carotid intima-media thickness in HIV infected patients. Med Ultrason 2011; 13(2):127–134. [PubMed: 21655539]
12. Pacheco AG, Grinsztejn B, da Fonseca Mde J, Moreira RI, Veloso VG, Friedman RK, et al. Traditional risk factors are more relevant than HIV-specific ones for carotid intima-media thickness (cIMT) in a Brazilian cohort of HIV-infected patients. PLoS One 2015; 10(2):e0117461. [PubMed: 25692764]
13. Mangili A, Polak JF, Quach LA, Gerrior J, Wanke CA. Markers of atherosclerosis and inflammation and mortality in patients with HIV infection. Atherosclerosis 2011; 214(2):468–473. [PubMed: 21130995]

14. Jotwani V, Scherzer R, Choi A, Szczech L, Polak JF, Kronmal RA, et al. Reduced kidney function and preclinical atherosclerosis in HIV-infected individuals: the study of fat redistribution and metabolic change in HIV infection (FRAM). American journal of nephrology 2011; 33(5):453–460. [PubMed: 21508633]
15. Grunfeld C, Delaney JA, Wanke C, Currier JS, Scherzer R, Biggs ML, et al. Preclinical atherosclerosis due to HIV infection: carotid intima-medial thickness measurements from the FRAM study. AIDS 2009; 23(14):1841–1849. [PubMed: 19455012]
16. Falcao Mda C, Zirpoli JC, Albuquerque VM, Markman Filho B, Araujo NA, Falcao CA, et al. Association of biomarkers with atherosclerosis and risk for coronary artery disease in patients with HIV. Arquivos brasileiros de cardiologia 2012; 99(5):971–978. [PubMed: 23080223]
17. Budoff MJ, Hokanson JE, Nasir K, Shaw LJ, Kinney GL, Chow D, et al. Progression of coronary artery calcium predicts all-cause mortality. JACC Cardiovasc Imaging 2010; 3(12):1229–1236. [PubMed: 21163451]
18. Inker LA, Schmid CH, Tighiouart H, Eckfeldt JH, Feldman HI, Greene T, et al. Estimating glomerular filtration rate from serum creatinine and cystatin C. The New England journal of medicine 2012; 367(1):20–29. [PubMed: 22762315]
19. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009; 150(9):604–612. [PubMed: 19414839]
20. Selzer RH, Hodis HN, Kwong-Fu H, Mack WJ, Lee PL, Liu CR, et al. Evaluation of computerized edge tracking for quantifying intima-media thickness of the common carotid artery from B-mode ultrasound images. Atherosclerosis 1994; 111(1):1–11. [PubMed: 7840805]
21. Stein JH, Brown TT, Ribaudo HJ, Chen Y, Yan M, Lauer-Brodell E, et al. Ultrasonographic measures of cardiovascular disease risk in antiretroviral treatment-naive individuals with HIV infection. Aids 2013; 27(6):929–937. [PubMed: 23196938]
22. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr., Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990; 15(4):827–832. [PubMed: 2407762]
23. Odden MC, Scherzer R, Bacchetti P, Szczech LA, Sidney S, Grunfeld C, et al. Cystatin C level as a marker of kidney function in human immunodeficiency virus infection: the FRAM study. Arch Intern Med 2007; 167(20):2213–2219. [PubMed: 17998494]
24. Hanna DB, Guo M, Buzkova P, Miller TL, Post WS, Stein JH, et al. HIV Infection and Carotid Artery Intima-media Thickness: Pooled Analyses Across 5 Cohorts of the NHLBI HIV-CVD Collaborative. Clin Infect Dis 2016; 63(2):249–256. [PubMed: 27118787]
25. Hsue PY, Ordovas K, Lee T, Reddy G, Gotway M, Schnell A, et al. Carotid intima-media thickness among human immunodeficiency virus-infected patients without coronary calcium. Am J Cardiol 2012; 109(5):742–747. [PubMed: 22169125]
26. Johnsen S, Dolan SE, Fitch KV, Kanter JR, Hemphill LC, Connelly JM, et al. Carotid intimal medial thickness in human immunodeficiency virus-infected women: effects of protease inhibitor use, cardiac risk factors, and the metabolic syndrome. J Clin Endocrinol Metab 2006; 91(12):4916–4924. [PubMed: 17003092]

Table 1.

Relationships between eGFR (using 3 CKD-EPI equations) and CIMT in HIV-positive and HIV-negative Individuals.

	CIMT					
	Cr Model		CysC Model		Cr-CysC Model	
	β (95% CI)[a]	P-value	β (95% CI)[a]	P-value	β (95% CI)[a]	P-value
Overall cohort						
HIV status (+/−)	126.33 (12.95, 239.72)	0.029	11.91 (−121.35, 145.16)	0.861	79.78 (−59.37, 218.93)	0.262
HIV− eGFR (mL/min/1.73m^2)	0.74 (−0.27, 1.76)	0.152	−0.40 (−1.47, 0.67)	0.465	0.06 (−1.12,1.24)	0.923
HIV+ eGFR (mL/min/1.73m^2)	−0.58 (−1.27, 0.11)	0.099	−0.61 (−1.23, 0.01)	0.055	−0.78 (−1.48, −0.08)	0.029
HIV*eGFR interaction	−1.32 (−2.49, −0.15)	0.027	−0.21 (−1.40, 0.98)	0.729	−0.84 (−2.15, 0.48)	0.213
HIV+ only						
eGFR (mL/min/1.73m^2)	−0.74 (−1.50, 0.01)	0.055	−0.64 (−1.33, 0.05)	0.069	−0.90 (−1.67, −0.13)	0.023

Abbreviations: CIMT, Carotid Intima Media Thickness; Cr, Creatinine; CysC, Cystatin C; eGFR, estimated glomerular filtration rate based on CKD-EPI equations using either Creatinine, Cystatin C, or both

[a]In the overall cohort, the β-coefficients are from a multivariable regression model including eGFR (per 1 mL/min/1.73^2), HIV status (positive vs. negative), and the interaction between eGFR and HIV status on the level of CIMT (in μm). Variables included in all models include age, race/ethnicity, sex, smoking status, body mass index, high density lipoprotein-cholesterol, low density lipoprotein-cholesterol, total cholesterol, triglycerides, systolic and diastolic blood pressures, history of diabetes, and Hepatitis C serostatus. Similar regression models were then constructed to assess the relationships between eGFR and CIMT using just HIV+ participants including several HIV-specific variables such as history of antiretroviral use, CD4 cell count and HIV-1 RNA level.

J Acquir Immune Defic Syndr. Author manuscript; available in PMC 2021 February 12.

Table 2.

Relationships between eGFR (using 3 CKD-EPI equations) and Coronary Artery Calcification in HIV-positive and HIV-negative Individuals.

	CAC (+/−)					
	Cr Model		CysC Model		Cr-CysC Model	
	β (95% CI)[a]	P-value	β (95% CI)[a]	P-value	β (95% CI)[a]	P-value
Overall cohort						
HIV status (+/−)	0.077 (0.001,8.458)	0.286	0.025 (0.000,8.386)	0.215	0.032 (0.000,8.936)	0.233
HIV− eGFR (mL/min/1.73m^2)	0.986 (0.945,1.028)	0.5	0.968 (0.921,1.017)	0.197	0.973 (0.927,1.021)	0.268
HIV+ eGFR (mL/min/1.73m^2)	1.003 (0.986,1.020)	0.729	0.994 (0.978,1.010)	0.468	0.997 (0.979,1.015)	0.734
HIV*eGFR interaction	1.018 (0.973,1.064)	0.443	1.027 (0.976,1.082)	0.307	1.025 (0.974,1.078)	0.349
HIV+ only						
eGFR (mL/min/1.73m^2)	1.003 (0.985,1.021)	0.758	0.992 (0.975,1.009)	0.364	0.996 (0.978,1.015)	0.699
	CAC $\log_{10}$ Agat					
	Cr Model		CysC Model		Cr-CysC Model	
	β (95% CI)[a]	P-value	β (95% CI)[a]	P-value	β (95% CI)[a]	P-value
Overall cohort						
HIV status (+/−)	169.41 (−1925.19, 2264.0)	0.874	443.47 (−2078.79, 2965.74)	0.731	392.28 (−2235.71,3020.26)	0.770
HIV− eGFR (mL/min/1.73m^2)	4.18 (−13.83,22.18)	0.650	−8.57 (−27.94,10.79)	0.388	−3.47 (−23.55,16.62)	0.736
HIV+ eGFR (mL/min/1.73m^2)	3.82 (−4.52,12.15)	0.371	−9.72 (−17.46,−1.97)	0.016	−3.64 (−12.49,5.20)	0.421
HIV*eGFR interaction	−0.36 (−19.56,18.83)	0.971	−1.14 (−21.29,19.00)	0.912	−0.17 (−21.28,20.93)	0.987
HIV+ only						
eGFR (mL/min/1.73m^2)	3.40 (−4.96,11.77)	0.427	−8.63 (−16.49,−0.77)	0.034	−2.83 (−11.78,6.12)	0.537

Abbreviations: Cr, Creatinine; CysC, Cystatin C; eGFR, estimated glomerular filtration rate based on CKD-EPI equations using either Creatinine, Cystatin C, or both; CAC log Agat, Coronary Artery Calcium $\log_{10}$ Agatson score; CAC(+/−), Coronary Artery Calcium detectable/nondetectable.

[a]In the overall cohort, the β-coefficients are from a multivariable regression model including eGFR (per 1 mL/min/1.73^2), HIV status (positive vs. negative), and the interaction between eGFR and HIV status on the level of CAC ($\log_{10}$ Agatson score or as detectable vs. nondetectable). Variables included in all models include age, race/ethnicity, sex, smoking status, body mass index, high density lipoprotein-cholesterol, low density lipoprotein-cholesterol, total cholesterol, triglycerides, systolic and diastolic blood pressures, history of diabetes, and Hepatitis C serostatus. Similar regression models were then constructed to assess the relationships between eGFR on CAC using just HIV+ participants including several HIV-specific variables such as history of antiretroviral use, CD4 cell count and HIV-1 RNA level.